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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/767,421	01/22/2001	Michael J. Shamblott	JHU1750-1	9551

7590 01/06/2010

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
01/06/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/767,421	SHAMBLOTT ET AL.	
	Examiner	Art Unit	
	Deborah Crouch	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,10,11,13,15,16,22,23,25-29,32 and 35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *22,23,25-29,32 and 35-37* is/are allowed.

6)☒ Claim(s) *1,10,13,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *January 22, 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's arguments filed September 28,. 2009 have been fully considered but they are not persuasive. Claims 1, 10, 13, 15, 16, 22, 23, 25-29, 32 and 35-37 are pending. The term “EBD-derived cell” means an undifferentiated cell that composes an embryoid body.

The rejection of claims 22, 23, 25-29, 32 and 35-37 under 35 U.S.C. § 112, written description in the office action mailed May 26, 2009 is withdrawn in view of applicant’s amendment to claim 22..

Claims 22, 23, 25-29, 32 and 35-37 are allowable.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 10, 13, 15, 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,453,357 issued September 26, 1995 (Hogan) in view of Shamblott et al (1998) Proced. Natl. Acad. Sci. 95, pp. 13726-13731 (ref. AE) for reasons set forth in the office action mailed May 26, 2009

Hogan teaches mouse embryoid body-derived cells (EBD) produced by plating mouse embryoid bodies on tissue culture plastic (col. 8, lines 42-45). The EBD cells are described as rapidly attaching to the plastic and give rise to a variety of cell types,

including endoderm, spontaneously contracting muscle, nerve and endothelial cells, and fibroblast like cells (col. 8, lines 45-49). Hogan describes the picking of single clones of mouse ES cells to, indicating clonal selection from a single EB-derived cell (col. 8, lines 5-9). These cell lines were then used to produce EBD cells in vitro. Further, the specification does not provide guidance as to characteristics of the claimed clonal EBD cells that would distinguish from the EBD cells of Hogan. Hogan offers additional motivation in stating derivatives of human ES cells, produced by the method disclosed therein, EBD-cells are a derivative of ES cells, could treat neurodegenerative disease (col. 5, lines 32-34). It is noted Hogan describes the EBD cells produced to contain a population of nerve cells. Hogan further teaches that LIF may not be required for the maintenance of ES cells, which are interpreted to be the cells of the claims (col. 4, lines 55-67). As a distinction between the claimed EBD's and those of Hogan cannot be seen, the characteristics of the EBD cells claimed would reasonably be expected to be present in Hogan's EBD cells.

Shamblott teaches embryoid bodies (EB's) produced from human primordial germ cells were plated into tissue culture plates in the absence of LIF (hPGC's) (13727, col. 1, parag. 2). After culture for 14 days, the EB's were shown to have developed into a variety of cell types – muscle, neurofilament (page 13729, Table 1).

As the presently claimed EBD cells are derived from human primordial germ cells, the ordinary artisan at the time of filing would have reasonably expected the physiological characteristics to be the same for the claimed cells and those of Hogan even given species differences. Thus, the cells of Hogan in view of Shamblott undergo

at least 30 population doublings, proliferate under culture conditions lacking LIF, a fibroblast feeder layer, or both, and transfectable with a retrovirus, lentivirus or both. There is no evidence to the contrary on the record. Products obvious over those in the art would be expected to have the same properties absent evidence to the contrary. It is noteworthy that the EBD cells claimed have been shown to consist of a variety of differentiated cell types just as the EBD cells of Hogan. This adds even more evidence that the EBD cells of the claims and those of Hogan in view of Shamblott are obvious. the ordinary artisan would have been motivated to produce human EBD cells as taught by Hogan in view of Shamblott to provide a source of lineage restricted cells for transplantation studies or developmental/differentiation research.

Therefore at the time of the present invention, it would have been obvious to produce human EBD-cells in view of the production of mouse EBD-cells as taught by Hogan in view of Shamblott teachings human EB's. The prior art offers the requisite teachings, suggestions and motivation to combine, and a reasonable expectation of success.

Applicant argues the claims are directed to EBD cells characterized by forming disaggregated single cells upon dissociation for EB's and adhering to defined extracellular matrix components lacking a feeder layer and lacking LIF and having the ability to be maintained in culture on the defined extracellular matrix components for at least 30 population doublings without being immortal. Applicant argues the cited references do not teach all the claim limitations and thus one of skill in the art would not be motivated to combine the reference teachings. These arguments are not persuasive.

What is lacking in applicant's response is any evidence the EBD cells claimed and those produced following the combination of prior art will possess any structural differences that imbue patentable distinction. While the conditions outlined in applicant's arguments is evidence that the EBD cells claimed were produced by a different method and different characteristics were observed, this does not provide evidence that EBD cells produced by a combination of Hogan and Shamblott would not have these same characteristics when isolated by the method stated in the claims.

Applicant argues the Examiner has mischaracterized Hogan. It is true the passage cited in the previous office action is incorrect. Applicant argues Hogan never produced EBD cells, but only cells derived from embryos. Applicant argues even if Hogan meant to isolate mouse EBD cells, this would not provide the claimed human EBDs. This argument is not persuasive.

Hogan col. 8, lines 38-49 is repeated below and emphasized. Clearly Hogan states undifferentiated cells (EG cells) were derived from embryos and cultured on feeder cells, trypsinized and plated bacteriological plastic dishes. These cells then formed EBs. When EBs were returned to tissue culture plastic, the EB cells attached to the plastic. There is no evidence of a structural difference between the EBD cells of Hogan and those of the present claims. While the cited prior art used a materially different and separate method of producing EBD cells, there is no evidence the EBD cells produced by either the art or the disclosed method isolated cells that were patentably distinct. The Examiner's issue is that there are two methods of producing

EBD cells, that of Hogan and Shamblott, and applicant's, but from the evidence of record they are the same cell.

Four independent lines of undifferentiated cells derived from 8.5 day embryos and cultured onto STO feeder layers were trypsinized and pipetted gently to generate small clumps of cells which were then placed in bacteriological plastic dishes. **After five to seven days most of the clumps differentiated into typical simple or cystic embryoid bodies (EBs), with a clear outer layer of extraembryonic endoderm cells (FIGS. 4, B).** ***When these EBs were returned to tissue culture plastic dishes they rapidly attached and over two weeks gave rise to a variety of cell types, including extraembryonic endoderm, spontaneously contracting muscle, nerve and endothelial and fibroblast-like cells.*** (Emphasis added.)

While mouse cells may have different characteristics that make them nonobvious to human EBD cells, this does not say using Shamblott's human embryos and Hogan's mouse method, human EBD's would not be produced having the characteristics argued.

Applicant argues Shamblott describes the derivation of pluripotent stem cells from germ cells and not from embryoid bodies. The cells taught by Hogan and Shamblott would require feeder layers for proliferation. These arguments are not persuasive.

Shamblott was used only to indicate the availability of human embryos for primordial germ cells, the starting tissue for Hogan's method, at the time of filing. While Hogan did not grow EBDs on feeder layers, this is not the same as saying Hogan's EBD's would not proliferate on feeder layers. A newly observed characteristic to an old product does allow for patentability to the old product. That is observing EBD cells proliferation on a feeder layer does not provide patentability for the known, Hogan's, EBD cells.

Applicant argues there is no motivation to combine Hogan and Shamblott as never references states a reason to produced EBD cells. This argument is not persuasive.

Hogan offers motivation for producing EBD cells to determine the characteristics of EG cells, if not for treatment.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/
Primary Examiner, Art Unit 1632

January 6, 2010